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EXAMINER

CHAKRABARTI, ARUN K

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8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/845,129

Applicant(s)
Duff

Examiner
Arun Chakrabarti

Art Unit
1655



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 4/27/01, 7/5/01, 8/30/01, 9/4/01, 9/17/01, 12/7/01, 12/26/01.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-57 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-57 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.

2. ☒ Certified copies of the priority documents have been received in Application No. 09/845,129.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

20) ☐ Other:

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DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Great Britain on May 21, 1998.

Double Patenting

2. Claims 1-6 and 8-57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 8-57 of U.S. Patent No. 6,268,142. (July 31, 2001). Although the conflicting claims are not identical, they are not patentably distinct from each other because the species of alleles of IL-1 inflammatory haplotype of U.S. Patent No.6,268,142 (claims 1, 8, 21, 29, 41, and 48) anticipate the genus IL-1 inflammatory haplotype (claims 1, 8, 21, 29, 41, and 48) of the instant application.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

4. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

5. Claim 7 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 7 of prior U.S. Patent No. 6,268,142. This is a double patenting rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6, and 8-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The specification discloses 22 alleles which corresponds to the cDNA/genomic DNA encoding the human species associated with the IL-1 polymorphism. Claims 1-6, and 8-57 are directed to encompass all gene sequences, sequences that hybridize to primers having SEQ ID NOs: 8-32, corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 8-32, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30

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USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for

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obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

Therefore, only SEQ ID NO: 8-32 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under

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35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-4, 8-10, 13-31 and 34-40 are rejected under 35 U.S.C. 103 (a)over Wang et al. (U.S. Patent 5,681,940) (October 28, 1997) in view of Duff et al. (U.S. Patent No. 5,698,399 (December 16, 1997) or alternatively in view of Bioque et al. (Clinical and Experimental Immunology, (1995), Vol. 102, pages 379-383).

Wang et al teaches a method for determining whether a subject has or is predisposed to developing a disease or condition that is associated with IL-1 comprising detecting at least one gene wherein the presence of the gene indicates that the subject is predisposed to the development or has the disease or condition (Column 7, lines 2-34 and).

Wang et al teaches a method wherein the disease of condition is selected from the group consisting of inflammatory disease, a degenerative disease, an immunological disorder, an infectious disease, a trauma induced disease, and a cancer (Column 7, lines 30-67).

Wang et al teaches a method wherein the detecting step is selected from the group consisting of hybridization and polymerase chain reaction and the like (Column 8, lines 1-

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9).

Wang et al teaches a method for determining the effectiveness of treating a subject that has or is predisposed to developing a disease or condition that is associated with an IL-1 polymorphism by detecting the level, amount or activity of mRNA in a sample obtained from the subject, administering the particular therapeutic to the subject, detecting the level of mRNA and comparing the relative levels (Column 7, lines 14-34).

Wang et al teaches a method for selecting an appropriate therapeutic for treating or preventing an individual that has or predisposed to developing a disease or disorder that is associated with an IL-1 polymorphism, comprising the steps of : detecting whether the subject contains the polymorphism and selecting a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the IL-1 polymorphism (column 8, lines 14-34 and Column 8, lines 1-9).

Wang et al teaches a method wherein the modulator activity of an IL-1 activity is an agonist or antagonist nucleic acid (column 7, lines 20-34).

Wang et al does not teach the association of disease condition with at least one allele of IL-1 inflammatory haplotype.

Duff et al teaches the association of disease condition with at least one allele of IL-1 inflammatory haplotype (Abstract).

Bioque et al teaches the association of disease condition with at least one

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allele of IL-1 inflammatory haplotype (Summary).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the IL-1 inflammatory haplotype associated disease detection model of Duff et al in the method of Wang et al. since Wang et al. states , “Oligonucleotides of the present invention are suitable for use in both in vivo and ex vivo therapeutic applications (Column 7, lines 35-36)”. An ordinary practitioner would have been motivated to combine the IL-1 inflammatory haplotype associated disease detection model of Duff et al or Bioque et al. in the method of Wang et al. in order to achieve the express advantages noted by Wang et al. of a system which can provide oligonucleotides suitable for use in both in vivo and ex vivo therapeutic applications.

10. Claims 41, 42, 44-56 are rejected under 35 U.S.C. 103 (a) over Potter et al. (U.S. Patent 5,780,587) (July 14, 1998) in view of Bioque et al. (Clinical and Experimental Immunology, (1995), Vol. 102, pages 379-383).

Potter et al teaches a method for screening for a therapeutic for treating or preventing a disease or condition that is associated with an IL-1 polymorphism comprising a proinflammatory haplotype (Abstract and column 2, lines 56 to column 3, line 12) comprising the steps of:

a) combining an IL-1 polypeptide or bioactive fragment thereof, an IL-1 binding partner and a test compound under conditions wherein, but for the test compound, the IL-1 protein and IL-1 binding partner are able to interact (Column 8, lines 55-67, column 15, lines

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15-59 and column 18, lines 15-44 and Example 5, Example 7 and Example 9 and Example 11).

b) detecting the extent to which, in the presence of the test compound, an IL-1 protein/IL-1 binding partner complex is formed, wherein an increase in the amount of complex formed by an agonist in the presence of the compound relative to in the absence of the compound or a decrease in the amount of complex formed by an antagonist in the presence of the compound relative to in the absence of the compound indicates that the compound is an effective therapeutic for treating or preventing the disease or condition (column 18, lines 1-44, column 15, lines 15-69, Figures 5 and 6, Example 5 and Example 9 and Example 11).

Potter et al teaches a method wherein the agonist or antagonist is selected from protein, peptides or nucleic acid (Example 5, Figure 5, column 15, lines 45-55 and Example 9).

Potter et al teaches a method wherein the polypeptide is IL-1Ra (Example 9, column 22, lines 54-55).

Potter et al teaches a method for identifying a therapeutic for treating or preventing a disease or condition that is associated with an IL-1 polymorphism that comprises an inflammatory haplotype (Abstract), comprising the steps of :

a) contacting an appropriate amount of a candidate compound with a cell or cellular extract, which express an IL-1 gene (Figures 5 and 6 and Examples 5 and 6).

b) determining the resulting protein bioactivity, wherein a decrease of an agonist bioactivity or a decrease in an antagonist bioactivity in the presence of the compound as

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compared to bioactivity in the absence of the compound indicates that the candidate is an effective therapeutic (Figures 5-9 and Examples 11 and 12).

Potter et al teaches a method wherein the protein bioactivity is determined by determining the expression level of an IL-1 gene (Example 11)

Potter et al teaches a method wherein the expression level is determined by detecting the amount of mRNA transcribed from an IL-1 gene (Examples 6 and 9).

Potter et al teaches a method wherein the expression level is determined using an anti-IL-1 antibody in an immunodetection assay (Example 11, lines 15-17).

Potter et al teaches a method which additionally comprises the step of preparing a pharmaceutical composition from the compound (column 17, lines 3-50).

Potter et al teaches a method wherein the cell is contained in an animal (Example 6).

Potter et al does not teach the association of disease condition with at least one allele of IL-1 inflammatory haplotype.

Bioque et al teaches the association of disease condition with at least one allele of IL-1 inflammatory haplotype (Summary).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the IL-1 inflammatory haplotype associated disease detection model of Bioque et al in the method of Potter et al. since Bioque et al. states, "These results suggests that the IL-1 beta/ IL-1Ra allelic cluster may participate in

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defining the biological basis of predisposition to chronic inflammatory bowel diseases (Summary, lines 21-23)". An ordinary practitioner would have been motivated to combine the IL-1 inflammatory haplotype associated disease detection model of Bioque et al. in the therapeutic screening method of Potter et al. in order to achieve the express advantages noted by Bioque et al. of a system which suggests that the IL-1 beta/ IL-1Ra allelic cluster may participate in defining the biological basis of predisposition to chronic inflammatory diseases..

11. Claims 1-4, 5, 8-11, 13-32 and 34-40 are rejected under 35 U.S.C. 103 (a) over Wang et al. (U.S. Patent 5,681,940) (October 28, 1997) in view of Bioque et al. (Clinical and Experimental Immunology, (1995), Vol. 102, pages 379-383) further in view of Weber et al. (U.S. Patent 5,582,979) (December 10, 1996).

Wang et al in view of Bioque et al. teach the method of claims 1-4, 8-10, 13-31 and 34-40 as described above.

Wang et al in view of Bioque et al do not teach the method wherein the amplification step employs a primer selected from the group consisting of any of SEQ ID Nos. 8-32.

Weber et al teach the method wherein the amplification step employs a primer selected from the group consisting of any of SEQ ID No. 8 (column 249, line 21, SEQ ID No. 247).

It would have been *prima facie* obvious to one having ordinary skill in the art

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at the time the invention was made to substitute and combine length polymorphism in certain sequences (SEQ ID NO. 247) and using the same model of Weber et al in the method of Wang et al in view of Bioque et al. since Weber et al. states , “The polymorphisms can be used to identify individuals as in paternity and forensic testing, and can be used to map genes which are involved in genetic diseases or in other economically important traits (Abstract, lines 3-6)”. An ordinary practitioner would have been motivated to combine SEQ ID NO. 247 model of Weber et al in the method of Wang et al. in view of Bioque et al in order to achieve the express advantages noted by Weber et al. of a system which can be used to map genes which are involved in genetic diseases or in other economically important traits.

12. Claims 1-4, 6, 8-10, 12-31 and 33-40 are rejected under 35 U.S.C. 103 (a) over Wang et al. (U.S. Patent 5,681,940) (October 28, 1997) in view of Bioque et al. (Clinical and Experimental Immunology, (1995), Vol. 102, pages 379-383) further in view of Yamada et al. (U.S. Patent 5,582,979) (December 10, 1996).

Wang et al in view of Bioque et al. teach the method of claims 1-4, 8-10, 13-31 and 34-40 as described above.

Wang et al in view of Bioque et al. does not teach a method wherein the size analysis is preceded by a restriction enzyme digestion.

Yamada et al teaches a method wherein the size analysis is preceded by a restriction enzyme digestion (Example 2, column 21, lines 20-41).

It would have been *prima facie* obvious to one having ordinary skill in the art

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at the time the invention was made to substitute and combine the size analysis preceded by a restriction enzyme digestion model of Yamada et al in the method of Wang et al in view of Bioque et al. since Yamada et al. states , “This invention relates to a DNA encoding a polypeptide having interleukin activity, a vector having the DNA inserted therein, a host transformed with the vector, a polypeptide having interleukin 1 activity which is produced by cultivation of the transformed host, derivatives of the polypeptide, a pharmaceutical composition containing the polypeptide or derivative, their use as an antitumor or antinfectious agent, and processes for the preparation thereof (Column 1, lines 9-17)”. An ordinary practitioner would have been motivated to combine the size analysis preceded by a restriction enzyme digestion model of Yamada et al in the method of Wang et al in view Bioque et al. in order to achieve the express advantages noted by Yamada et al. of a system which can provide DNA encoding a polypeptide having interleukin activity.

13. Claims 41-56 are rejected under 35 U.S.C. 103 (a) over Potter et al. (U.S. Patent 5,780,587) (July 14, 1998) in view of Bioque et al. (Clinical and Experimental Immunology, (1995), Vol. 102, pages 379-383) further in view of Wang et al. (U.S. Patent 5,681,940) (October 28, 1997) .

Potter et al in view of Bioque et al teach the method of claims 41, 42, 44-56 as described above.

Potter et al in view of Bioque et al do not teach the method wherein the nucleic acid is selected from the group consisting of : an antisense, ribozyme and triplex nucleic

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acid.

Wang et al teaches the method wherein the nucleic acid is selected from an antisense nucleic acid (column 7, lines 14-27).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the antisense nucleic acid model of Wang et al in the drug screening method of Potter et al in view of Bioque et al since Wang et al. states , “Oligonucleotides of the present invention are suitable for use in both in vivo and ex vivo therapeutic applications (Column 7, lines 35-36)”. An ordinary practitioner would have been motivated to combine the antisense nucleic acid model of Wang et al in the drug screening method of Potter et al in view of Bioque et al in order to achieve the express advantages noted by Wang et al. of a system which can provide oligonucleotides suitable for use in both in vivo and ex vivo therapeutic applications.

14. Claims 41, 42 and 44-57 are rejected under 35 U.S.C. 103 (a) over Potter et al. (U.S. Patent 5,780,587) (July 14, 1998) in view of Bioque et al. (Clinical and Experimental Immunology, (1995), Vol. 102, pages 379-383) further in view of Yoneda et al. (U.S. Patent 5,993,817) (November 30, 1999).

Potter et al in view of Bioque et al teach the method of claims 41, 42, 44-56 as described above.

Potter et al in view of Bioque et al do not teach the method wherein the animal is transgenic.

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Yoneda et al teaches the method wherein the nucleic acid is selected from an antisense nucleic acid (column 2, lines 40-67).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the transgenic mice model of Yoneda et al in the drug screening method of Potter et al. in view of Bioque et al since Yoneda et al. states , “It has also been shown that transgenic mice that are modified to comprise an IL-6 gene knockout show reduced bone loss in models for osteoporosis (Column 2, lines 56-59)”. An ordinary practitioner would have been motivated to combine the transgenic mice model of Yoneda et al in the drug screening method of Potter et al. in view of Bioque et al in order to achieve the express advantages noted by Yoneda et al. of a transgenic mice model with interleukin gene knockout which shows reduced manifestation of a degenerative disease.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number

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for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Arun Chakrabarti,

Patent Examiner,

February 25, 2002

Arun K. Chakrabarti
ARUN K. CHAKRABARTI
PATENT EXAMINER